

***For Vagus Nerve Stimulation
with the VNS Therapy™ System***

March 2004

This Patient's Manual is a supplement to the physician's manuals. It is not meant to take the place of advice from your doctor. For a complete discussion of indications for use, contraindications, precautions, warnings, and potential side effects, please talk to your doctor.

Please talk with your doctor about

- ?? how this device is used
- ?? how it should not be used
- ?? safety measures
- ?? warnings
- ?? side effects

Your doctor's phone number:



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Useful Terms

These terms are used in this manual.

Adjunctive — Additional

Adverse events — Complications and side effects

Clinical benefit — Categories assigned to describe change in depressive symptoms on Hamilton Rating Scale for Depression-24 Item after VNS Therapy

Meaningful clinical benefit – 25% to 49% improvement in depressive symptoms

Highly meaningful clinical benefit – 50% to 74% improvement in depressive symptoms

Extraordinary clinical benefit – over 75% improvement in depressive symptoms

Clinical studies — Tests of the effectiveness and safety of a therapy on humans

Cyberonics — Company that makes the VNS Therapy System

Electrodes — Part of the VNS Therapy Lead that connects to the vagus nerve

HSRD₂₄ — Standardized test to measure depressive symptoms as reported by the doctor; Hamilton Rating Scale for Depression-24 Item

ISD-SR — Standardized test to measure depressive symptoms as reported by the patient, Inventory of Depressive Symptomatology Self-Report

Lead — VNS Therapy Lead; small wire that connects the VNS Therapy Pulse Generator to the vagus nerve

MADRS — Standardized test to measure depressive symptoms as reported by the doctor, Montgomery Ashberg Depression Rating Scale; commonly used in Europe

Programming Wand — VNS Therapy instrument used to check or change VNS Therapy device and settings

Pulse Generator — VNS Therapy device implanted in the patient's chest; holds the battery and delivers stimulation to the vagus nerve through the VNS Therapy Lead

Reed Switch — This mechanism works like a gate. When the Magnet closes it, the signal (stimulation) cannot pass. The Pulse Generator is temporarily turned OFF.

Remitter — Study participant who was essentially free of depressive symptoms after receiving VNS Therapy; determined by scores of standardized tests; also called complete responder

Responder — Study participant whose depressive symptoms were reduced by 50% or more after receiving VNS Therapy; determined by scores of standardized tests

Stimulate — Send electrical signal; with VNS Therapy, the Pulse Generator sends an electrical signal through the Lead to the vagus nerve, which carries the signal to the brain

Stimulation — The electrical signal that is sent from the Pulse Generator to the brain

Treatment-resistant Depression (TRD) — Depression that has not responded to two or more antidepressant treatments

Vagus nerve — A nerve that extends from the brain through the neck to the major organs (heart, lungs, stomach, etc.) in the torso

Vagus Nerve Stimulation — (VNS) periodic electrical signals sent from the Pulse Generator to the vagus nerve

VNS Therapy — Treatment received from vagus nerve stimulation

VNS Therapy System — All of the parts that provide VNS Therapy: Pulse Generator, Lead, Programming Wand, Computer, Software, and Magnets

1. INTRODUCTION TO VNS THERAPY

Many people have depression. Through the years, doctors and scientists have learned much about depression. They have developed drugs and other treatments. Despite these efforts, some people still have depression. Your doctor has proposed the VNS Therapy™ System for you to reduce the symptoms of your depression because drugs either have failed to control them adequately or have caused intolerable side effects.

The VNS Therapy System sends a mild electrical impulse to a nerve that goes to the brain. This nerve is called the vagus nerve. The treatment is Vagus Nerve Stimulation (VNS) Therapy (VNS Therapy™).

Note: Name Change —In the past, the device and its parts were called the NeuroCybernetic Prosthesis (or NCP) System. The NCP System has been renamed the VNS Therapy System. Throughout this manual, the term VNS Therapy System includes the NCP System.

Vagus means “wanderer” in Latin. The vagus nerve is well named. In adults, it is about 56 centimeters long (22 inches). It wanders throughout the upper body. The major organs of the body communicate with the brain

through the vagus nerve. The vagus nerve forms a good electrical connection with the brain for several reasons.

?? There are few if any pain fibers in the vagus nerve.

?? Over 80% of the electrical signals applied to the vagus nerve in the neck travel to the brain.

?? Attaching the VNS electrode to the vagus nerve does not involve the brain directly; it is not brain surgery.

2. HOW THE VNS THERAPY SYSTEM WORKS

2.1. Parts of the VNS Therapy System

The VNS System has several implantable and nonimplantable parts (see Figures 1 and 2).

2.1.1. Implantable parts

?? VNS Therapy Pulse Generator

?? VNS Therapy Lead

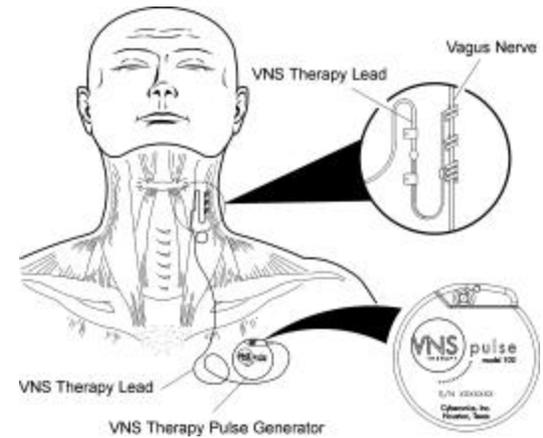


Figure 1. Implantable parts of the VNS Therapy System

2.1.2. Nonimplantable parts

- ?? VNS Therapy Computer
- ?? VNS Therapy Software
- ?? VNS Therapy Programming Wand
- ?? VNS Therapy Magnets

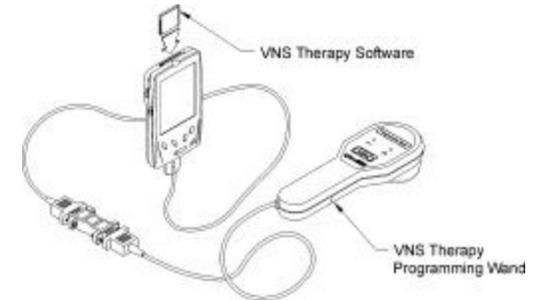


Figure 2. Nonimplantable parts of the VNS Therapy System

2.1.3. Pulse Generator

The main part is the Pulse Generator, sometimes called a stimulator. Similar to cardiac pacemakers, which have been used since 1958 to control heart problems, the Pulse Generator is computer controlled and battery powered. It sends signals through the electrodes of the Lead to the brain by way of the left vagus nerve.

2.1.4. Placement of the Pulse Generator and Lead

The Pulse Generator is placed under the skin of the upper chest. The Lead connects the Pulse Generator to the vagus nerve. It attaches to the vagus nerve on the left side of the neck. The Pulse Generator and Lead are implanted by a surgeon during an operation that typically lasts from about 45 minutes to 2 hours. Later, your doctor sets the Pulse Generator to deliver periodic stimulation 24 hours a day (for example, 30 minutes ON and 5 minutes OFF). At the office, your doctor can read and change stimulation settings with the Computer, Software, and Programming Wand.

2.1.5. Cyberonics Magnet

Cyberonics provides a Magnet for you to stop the stimulation when it is needed (see “To stop stimulation” in the Using Your Cyberonics Magnets section of this manual).

2.1.6. Stimulation settings

The Pulse Generator has many settings. Your doctor will choose the settings. He or she can change (reprogram) the periodic stimulation at any time with the Programming Wand, Software, and Computer. Most of the time, changing the VNS Therapy System settings is a painless

procedure, takes only a few minutes, and can be done in the doctor's office.

2.1.7. Pulse Generator life

The Pulse Generator can last from 1 to 16 years

The lifespan depends on these factors.

?? Pulse Generator model

?? Settings your doctor chooses

?? Interaction of the Lead and vagus nerve over time

At typical settings, battery life ranges from 6.6 to 10 years. Ask your doctor for more details about your device and settings.

When the battery in your Pulse Generator runs out, the Pulse Generator can be replaced in an outpatient operation. The operation involves anesthesia, and takes less than an hour to complete.

Your doctor will set the Pulse Generator to periodically stimulate 7 days a week, 24 hours a day. One typical "dose" is stimulation of about 30 seconds ON and 5 minutes OFF. (Your settings could vary.) This dose remains until your

doctor changes the Pulse Generator settings or the battery runs out.

2.1.8. Stopping the stimulation

At any time, you can stop the stimulation with a Cyberonics Magnet (see the “Using Your Cyberonics Magnets” sections of this manual).

3. QUICK REFERENCE GUIDE

This quick guide provides important information about the VNS Therapy System. It will be most useful after you have read the whole manual. A list of frequently asked questions is included at the end of this manual.

When you see this symbol , pay special attention to the important information after it.

After you receive your VNS Therapy System, keep this important information in mind.

- ?? **Use the Cyberonics Magnet to stop the stimulation** if it becomes painful or irregular (see the “To Stop Stimulation” section).
- ?? **Call your doctor right away** if any of the following occur.
 - ?? your voice is constantly hoarse
 - ?? the stimulation becomes painful or irregular
 - ?? the stimulation causes any choking, trouble with breathing, trouble with swallowing, or change in heart rate
 - ?? you think that the Pulse Generator may not be stimulating properly or that the VNS Therapy System battery is depleted (stops stimulating)

- ?? you notice anything new or unusual that you relate to the stimulation
- ?? the feeling that you usually have during stimulation becomes stronger or weaker (see the “Complications” section)
- ?? your depressive symptoms increase. See the “Complications” and “Side Effects” sections of this manual for details.
- ?? Call your doctor before you have **any medical tests** (see the “Medical Hazards” section).
- ?? Call your doctor before you have **any other medical devices implanted** (see the “Medical Hazards” section).
- ?? Tell your doctor at your next visit if you no longer feel the routine stimulation. Your doctor may decide to change your settings.
- ?? Cyberonics *cannot* provide health care advice or services. Your source for health questions must always be your doctor.

4. WHO USES VNS THERAPY?

Doctors prescribe VNS Therapy for people with chronic or recurrent depression. It is *not* right for everyone who has depression. Your doctor will decide if VNS Therapy is right for you. Your doctor will also decide if you have any other medical conditions that might be affected by VNS Therapy.

4.1. Indications for Use

The VNS Therapy System is indicated for the adjunctive long-term treatment of chronic or recurrent depression for patients over the age of 18 who are experiencing a major depressive episode that has not had an adequate response to two or more adequate antidepressant treatments.

4.2. Contraindications (How VNS Therapy Should Not Be Used)

 **CONTRAINDICATION:** The VNS Therapy System should not be used (is contraindicated) in people who have had the left vagus nerve cut to treat another disorder (a left vagotomy).

 **CONTRAINDICATION:** Inform anyone treating you that you **CANNOT** have any short-wave diathermy, microwave diathermy, or therapeutic ultrasound diathermy (hereafter referred to as “diathermy”) anywhere on your body because you have an implanted VNS Therapy System (sometimes referred to as a “Vagus Nerve Stimulator” or “Vagus Nerve Stimulation”). **Diagnostic ultrasound is not included in this contraindication.**

Diathermy is a treatment to promote healing or relieve pain. It is provided by special medical equipment (diathermy equipment) in a doctor’s office, dentist’s office, or other healthcare setting.

Energy from diathermy therapy may cause heating of the VNS Therapy System. The heating of the VNS Therapy System resulting from diathermy can cause temporary or permanent nerve or tissue or vascular damage. This damage may result in pain or discomfort, loss of vocal cord function, or even possibly death if there is damage to blood vessels.

Diathermy may also damage parts of your VNS Therapy System. This damage can result in loss of therapy from your VNS Therapy System. More surgery may be required to remove or replace parts of your implanted device.

Injury or damage can occur during diathermy treatment whether your VNS Therapy System is turned “on” or “off.”

5. CLINICAL STUDY PARTICIPANTS

Safety and effectiveness studies involved a total of 295 men and women who received VNS Therapy along with their usual antidepressant treatments. Sixty of them participated in a feasibility study that compared depressive symptoms before and after VNS Therapy. The favorable results from the feasibility study prompted a pivotal study that compared 235 people who received VNS Therapy along with their other antidepressant treatments with 124 people who received antidepressant treatments, but not VNS Therapy. All of the study participants had chronic or recurrent depressive symptoms that had not responded to antidepressant treatments.

The typical person who received VNS Therapy in the pivotal study was about 46 years old, and had been diagnosed with depression at age 22 years. Two-thirds of study participants were women. The typical current depressive episode had continued for more than 4 years.

The safety of VNS Therapy was established previously during the clinical trials for the treatment of epilepsy, and, worldwide, more than

22,000 people have been implanted with the VNS Therapy device.

If you would like to learn more about the VNS studies, talk to your doctor.

5.1. Safety and Efficacy Unknown for These Conditions

The safety and efficacy of VNS Therapy has *not* been shown for people with these conditions.

- ?? History of gastric or duodenal ulcers
- ?? History of respiratory diseases or disorders
- ?? Pre-existing hoarseness
- ?? Other concurrent forms of brain stimulation
- ?? Cardiac (heart) arrhythmias or other abnormalities
- ?? Unstable medical conditions
- ?? Progressive neurological disease, including vasovagal syncope
- ?? Previous therapeutic brain surgery
- ?? Pregnancy or nursing*

VNS Therapy and pregnancy*

At this time, VNS Therapy has not been studied in pregnant women. Studies of pregnant rabbits showed no evidence of impaired fertility or harm to the fetus due to VNS Therapy. However, animal studies do not always predict human response and cannot address human development. VNS Therapy should be used during pregnancy only if clearly needed.

The operating ranges of the VNS Therapy System and fetal monitors are not the same and no interaction would be expected. No tests for interaction between the VNS Therapy System and fetal monitoring systems have been performed, so the systems could potentially interact.

6. BENEFITS OF VNS THERAPY

6.1. Reduced Depressive Symptoms

After 12 months of VNS Therapy, more than one in two persons had a meaningful benefit (? 25% in depressive symptoms) and almost one in six was essentially free of depressive symptoms. The success of VNS Therapy in decreasing depressive symptoms was demonstrated by improved scores on standardized tests after 12 months of VNS Therapy. Results of the Hamilton Rating Scale for Depression-24 (HRSD₂₄) showed that 30% of the participants were responders (? 50% in depressive symptoms) and 17% were remitters (minimal to no depressive symptoms). The Inventory of Depressive Symptomatology Self-Report (IDS-SR) showed that 22% of the group were responders and 15% were remitters. The Montgomery Ashberg Depression Rating Scale (MADRS) showed that 32% were responders and 24% were remitters. (See Table 1 and Figures 3 and 4.)

Table 1. Percent of Responders and Remitters After VNS Therapy

Standardized Test	HRSD ₂₄		IDS-SR		MADRS	
	Responders	Remitters	Responders	Remitters	Responders	Remitters
3 months	15%	7%	14%	6%	17%	10%
12 months	30%	17%	21%	16%	32%	23%

Responders - ?50% improvement in depressive symptoms.

Remitters – minimal to no depressive symptoms.

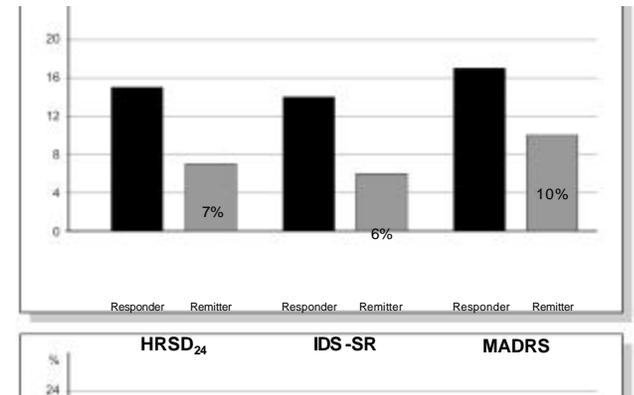


Figure 3. Responders and Remitters After VNS Therapy (3 months)

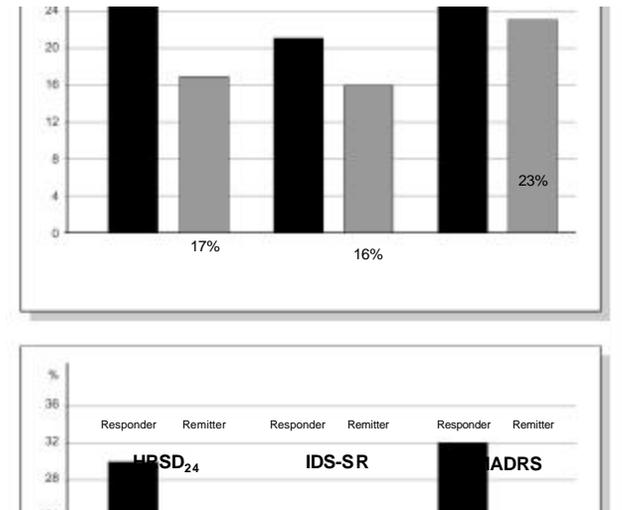


Figure 4. Responders and Remitters After VNS Therapy (12 months)

Clinical benefit was primarily evaluated according to changes in HRSD₂₄ scores. Of the study participants who received some level of meaningful clinical benefit after 3 months of VNS Therapy, 73% maintained at least a meaningful benefit after 12 months. Of the study participants who received no clinical benefit after 3 months of VNS Therapy, 47% received a meaningful clinical benefit after 12 months.

Long-term results from clinical studies show that the effects of VNS Therapy *are* significant and last over time.

6.2. Improved Quality of Life

Improvements other than decreased depressive symptoms were noted by study participants receiving VNS Therapy for 1 year and their doctors. Scores on the MOS SF-36, a test that measures quality of life, identified several areas that showed statistically significant (mathematically important) improvement.

?? Vitality (energy)

?? Social Functioning (social activities affected by physical or emotional problems)

?? Role Functioning-emotional (role activities affected by emotional problems)

?? Mental Health (psychological well-being)

6.3. Gradual Improvement

The benefits of VNS Therapy are not always seen right away. In fact, depressive symptoms may improve slowly over the first year of treatment. Long-term results from clinical studies show that the effects of VNS Therapy *are* significant and last over time.

6.4. Not a Cure for Depression

VNS Therapy has not been shown to cure depression. It does not work for everyone. At present, doctors have no way to predict which patients will respond to VNS Therapy.

7. HAVING THE DEVICE IMPLANTED

VNS Therapy requires surgical placement of the Pulse Generator and Lead by a surgeon. At office visits, your doctor checks the settings and changes them as needed.

7.1. Surgery (Operation)

Surgery lasts from about 45 minutes to 2 hours and typically involves general anesthesia, though local anesthesia is sometimes used. You will probably stay in the hospital overnight.

The surgeon makes a small incision below the collarbone in the chest or armpit. The Pulse Generator is placed in this surgically made “pocket.”

A second small incision is made in the neck for the Lead. The Lead is attached to the left vagus nerve in the lower side of the neck and to the Pulse Generator under the skin (Figure 1).

The operation can be reversed if you and your doctor ever decide to have the VNS Therapy System removed.

7.2. Follow-up

The Pulse Generator is usually started 2 weeks after it is implanted. (Your doctor will program the Pulse Generator to the proper settings for you.) At that office visit and at all others, your doctor will check the VNS Therapy System. Your doctor will make sure that it is working well and that the treatment is not uncomfortable for you.

 Cyberonics recommends that you see your doctor **at least once every 6 months. Your doctor will check the VNS Therapy System for safe and effective operation.**

You will be given an Implant and Warranty Registration Card. It has information about your Pulse Generator and Lead.

You will also receive a Patient Emergency Information Card. It has phone numbers to call in case of a device-related emergency.

 Carry the Patient Emergency Information Card at all times.

 Your doctor is your first source for health-related questions and information. Cyberonics *cannot* provide health care advice or services.

7.3. Antidepressant Medications (Drugs for Depression)

Most patients treated with VNS Therapy in the clinical studies continued to also take antidepressant medications.

Your doctor may advise you to continue taking your antidepressant medications after you begin receiving VNS Therapy. Over time, your doctor will decide whether to reduce your antidepressant medications. Always follow your doctor's instructions about your medications.

8. THE CYBERONICS MAGNETS

8.1. Handling the Cyberonics Magnets

After your operation, your doctor will give you two magnets. You should carry one of the Magnets with you at all times in your pocket, in your purse away from credit cards, or in another convenient place. If you prefer, you can wear them like a watch or a pager (see Figure 5).

If the Magnets are handled carefully, they should last many years.

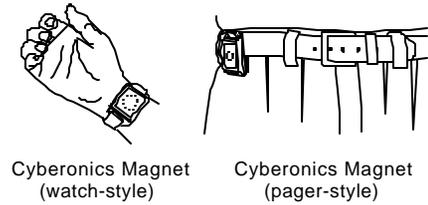


Figure 5. The Cyberonics Magnets

 **Never put or store the Magnets near credit cards ,** televisions, computers, computer disks, microwave ovens, watches, or other magnets. Keep them at least 10 inches (25 centimeters) away.

 **Do not drop the Magnets.** They can break if dropped on a hard surface.

 **Carry a Magnet with you at all times.** Show your family members or caregivers how to use the Magnet.

8.2. Using Your Cyberonics Magnets

Keep a Magnet with you at all times. You may need to turn OFF the Pulse Generator.

The Magnet can be used to stop stimulation temporarily or turn OFF the Pulse Generator

- ?? when you plan to sing or speak in public (if stimulation bothers you when you do this)
- ?? when you are eating (if you have swallowing problems)
- ?? if stimulation becomes uncomfortable or painful

 The correct position for the Magnet may vary from patient to patient. The position depends on how the Pulse Generator is implanted. Find the position that works best for you.

8.2.1. To stop stimulation

1. Put the Magnet over the Pulse Generator (see Figure 6). If the stimulation stays on, move the Magnet around until it stops.

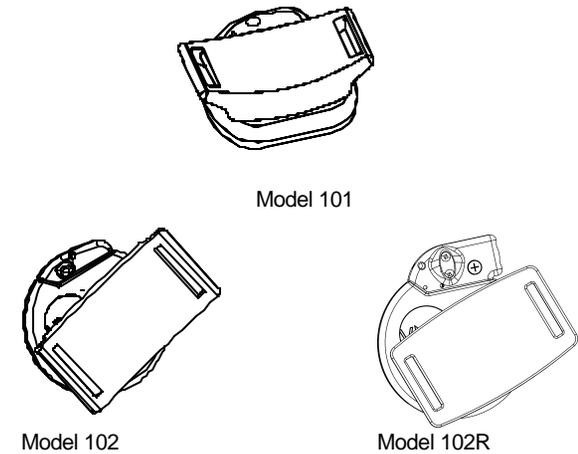


Figure 6. Stopping Stimulation

Note: To show the correct position of the Magnet with the Pulse Generator, the Magnet has been drawn without the belt clip or wristband. The belt clip and wristband use the same Magnet.

2. Leave the Magnet over the Pulse Generator. If needed, tape it to your chest or use an elastic, wrap-around bandage.

3. If you stopped the stimulation because it was painful or felt unusual, call your doctor right away.

The Pulse Generator will not stimulate while the Magnet is in place, but it will start when the Magnet is removed.

8.3. How the Magnets Work

The VNS Therapy System senses a magnetic field. Holding a Magnet over the Pulse Generator causes a **Reed Switch** inside the Pulse Generator to close. This switch works like a gate. When the Magnet closes it, the signal (stimulation) cannot pass. The Pulse Generator is temporarily turned OFF.

When the Magnet is removed, the switch (gate) opens right away. The VNS Therapy System is turned back ON and can stimulate again.

8.3.1. Finding the Reed Switch

You may need to move the Magnet around to find the Reed Switch and stop stimulation (Figure 6).

The label side of the Magnet should face the Reed Switch. Figure 7 shows the position of the switch.

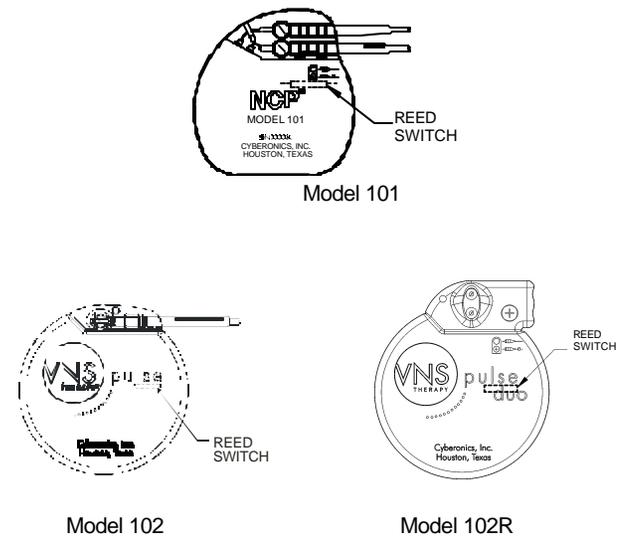


Figure 7. Reed Switch Position

8.3.2. Know your Magnets

These tips are also given elsewhere in these instructions. Be sure that you understand them.

- ?? **Use the Magnet *only when necessary to turn off stimulation.***
- ?? **With your doctor's permission, it is okay to leave the Magnet in place** for a short while, for example, to sing a song. The Pulse Generator will not stimulate while the Magnet is in place. The stimulation cycle begins again when the Magnet is removed.
- ?? **If stimulation hurts**, hold the Magnet over the Pulse Generator and keep it there. The stimulation will stop as long as the Magnet is there. If necessary, tape the Magnet in place. Contact your doctor right away.
- ?? **Always carry the Magnet with you.** If you have pain because of stimulation, you can stop it by placing the Magnet over the Pulse Generator.
- ?? Keep the Magnets away from credit cards, computer disks, watches, and other items affected by strong magnetic fields.
- ?? **If you lose one of your Magnets**, you may buy a new one from Cyberonics. A Magnet Order Form is included in your Patient Essentials Kit. You may also buy new Magnets by contacting Cyberonics' Customer Service department (see number on back cover of this manual).

?? **And remember—if you are not sure about using the Magnets, ask your doctor to show you how.**

8.4. Replacing the Cyberonics Magnets

To order a new Magnet, contact Cyberonics' Customer Service department at the number on the back cover of this manual. A Magnet Order Form, with prices, is included in your Patient Essentials Kit. You may also request a copy of this Patient's Manual.

9. WARNINGS, PRECAUTIONS, AND CONTRAINDICATIONS

As with all types of treatment for depression, vagus nerve stimulation carries some risks. Talk to your physician about other risks not covered in this manual that you should know about. Also be sure to ask any questions that you have about any of the following warnings, precautions, side effects, and possible hazards.

9.1. Warnings

With your doctor, review the warnings that follow, as well as any other issues that concern you.

 **Be aware that aspiration (inhaling fluid into the lungs) can result** from the increased swallowing difficulties reported by some people during stimulation. People who have pre-existing swallowing problems are at greater risk for aspiration.

 **Use the Magnet to stop stimulation** if you suspect that the Pulse Generator is not working properly or if stimulation is painful. Then, immediately contact your physician. If the VNS Therapy System stops working properly, additional surgery may be required.

 **Contact your doctor immediately** if you notice a constant hoarseness within a few days after surgery. Implantation of the Lead may cause nerve constriction (squeezing of the nerve).

 Patients diagnosed with obstructive sleep apnea (OSA) may experience increased breathing problems while asleep during VNS stimulation. If you have OSA and experience a worsening of your breathing problems during sleep, notify your physician.

9.2. Precautions

In addition to the warnings in the previous section, pay special attention to these precautions.

 **Throat pain may result from stimulation.** People who smoke may have an increased risk of throat pain.

 **Shortness of breath may result from stimulation.** People with chronic pulmonary disease (breathing difficulties) may have an increased risk of shortness of breath from stimulation. This side effect may be more noticeable during strenuous exercise.

 **If stimulation stops, your depressive symptoms may increase** to levels greater than those before stimulation started. Contact your doctor if you notice this happening.

 During device implantation, abnormal **cardiac (heart) rhythm changes have occurred** in some (about 1 per 1,000) patients. No deaths have occurred from these abnormalities.

9.3. Contraindications (How VNS Therapy Should Not Be Used)

 **CONTRAINDICATION:** The VNS Therapy System should not be used (is contraindicated) in people who have had the left vagus nerve cut to treat another disorder (a left vagotomy).

 **CONTRAINDICATION:** Inform anyone treating you that you **CANNOT** have any short-wave diathermy, microwave diathermy, or therapeutic ultrasound diathermy (hereafter referred to as “diathermy”) anywhere on your body because you have an

implanted VNS Therapy System (sometimes referred to as a “Vagus Nerve Stimulator” or “Vagus Nerve Stimulation”). **Diagnostic ultrasound is not included in this contraindication.**

Diathermy is a treatment to promote healing or relieve pain that is provided by special medical equipment (diathermy equipment) in a physician’s office or dentist’s office or other healthcare office.

Energy from diathermy therapy may cause heating of the VNS Therapy System. The heating of the VNS Therapy System resulting from diathermy can cause temporary or permanent nerve, tissue, or vascular damage. This damage may result in pain or discomfort, loss of vocal cord function, or even possibly death if there is damage to blood vessels.

Diathermy may also damage parts of your VNS Therapy System. This can result in loss of therapy from your VNS Therapy System, and may require additional surgery to remove or replace parts of your implanted device. Injury or damage can occur during diathermy treatment whether your VNS Therapy System is turned “on” or “off.”

10. ADVERSE EVENTS (COMPLICATIONS AND SIDE EFFECTS)

Some complications and side effects may occur with vagus nerve stimulation. But doctors involved with the studies of VNS Therapy for depression rated most of the side effects as mild or moderate. Most side effects decrease over time. In addition, the Magnet can be used to stop stimulation temporarily or to turn OFF the Pulse Generator if stimulation becomes uncomfortable or painful.

If you are thinking about VNS Therapy, give thought to the risks. Learn as much as you can about the treatment.

If you have questions, talk to your doctor. Ask your doctor to explain other risks you should know about that are not covered in this manual.

10.1. Complications

Complications linked to the VNS Therapy System can result from

- ?? Surgery
- ?? Pulse Generator malfunction (not working)
- ?? Battery depletion (running out)
- ?? Touching or moving the device through the skin

10.1.1. Surgery

Like a heart pacemaker, the VNS Therapy device is implanted during surgery. One incision is made in the chest for the Pulse Generator. A second incision is made in the neck to place the Lead. All types of surgery carry some risks. With this type of surgery, the Pulse Generator and/or Lead can—but rarely does—move or come through the skin. Also, the Lead can break or become disconnected from the Pulse Generator.

10.1.1.1. *Infrequent Surgical Complications*

These surgical complications occur infrequently with the surgery required to implant the VNS Therapy System. They may be short-term or long-term. These complications include acute kidney failure, aspiration pneumonia, abnormal thinking, allergic reaction, asthenia (loss of bodily strength), chest pain, fever, infection, hemorrhage, palpitation, dizziness, hypertonia, insomnia, vocal cord paralysis, rash, urinary retention, and syncope.

 Implantation of the Lead may cause nerve constriction (squeezing of the nerve). Call your doctor right away if your voice is always hoarse a few days

after surgery. (There could be other explanations for this symptom.)

10.1.1.2. *Surgical side effects*

These surgical side effects were listed as related to the surgery required to implant the VNS Therapy device. These side effects were reported for 5% or more of the study participants.

- ?? Incision pain (36%)
 - ?? Voice alteration (33%)
 - ?? Incision site reaction (29%)
 - ?? Device site pain (23%)
 - ?? Device site reaction (14%)
 - ?? Pharyngitis (inflammation of the throat) (13%)
 - ?? Dysphagia (difficulty swallowing) (11%)
 - ?? Hypesthesia (numbness) (11%)
 - ?? Nausea (9%)
 - ?? Dyspnea (shortness of breath) (9%)
 - ?? Headache (8%)
 - ?? Neck pain (7%)
 - ?? Pain (7%)
 - ?? Increased cough (6%)
 - ?? Paresthesia (tingling sensation) (6%)
-

Most side effects linked with surgery lessened over time. The discomfort associated with surgery usually resolved within the first 3 months after surgery. Voice alteration may continue and is probably a side effect of stimulation.

10.1.1.3. *Surgical scars*

Scars from the surgery can be lessened. Talk to your surgeon if you have specific concerns.

10.1.2. **Pulse Generator malfunction (not working right)**

The Pulse Generator can malfunction, though this is rare. The stimulation from a Pulse Generator that is not working right can cause intense neck pain, hoarseness, choking, or trouble breathing.

 **Stimulation from a Pulse Generator that is not working right could damage the vagus nerve** and lead to permanent hoarseness or other complications. Malfunction of the Pulse Generator could cause the battery to run out sooner than expected. **If you have any of these symptoms**, or if stimulation becomes painful, irregular, or nonstop, place the Magnet over the Pulse Generator. Hold it there to stop stimulation (see “To stop stimulation” in the Using Your

Cyberonics Magnets section). Then **call your doctor right away.**

10.1.3. Battery depletion (running out)

The battery in your Pulse Generator will normally last between 6.6 to 10 years. The Pulse Generator battery will slowly lose its power when it starts to run out. It will begin to stimulate differently. You may sense this change as irregular stimulation. At the end, the stimulation will stop completely. (See the “Checking Stimulation” section for how to tell if the device is stimulating.)

 *After stimulation stops (when the Pulse Generator battery runs out), you may notice a change in your depressive symptoms. If you think that the Pulse Generator might not be working right, call your doctor.*

When the battery runs down, the Pulse Generator can be replaced in an outpatient surgery. Most of the time, the operation takes about 1 hour and uses local anesthesia.

Replacement or removal of the Lead is a different procedure. It is not required for routine replacement of the Pulse Generator.

10.1.4. Manipulation of the Pulse Generator and Lead

The Pulse Generator is secured into place during surgery, but the device can move (migrate) slightly. It may be possible to feel the Lead under the skin after surgery. This feeling is normal. It should become less apparent over time (several weeks). Manipulation of the Lead should be prevented at all times.

 Never move or twist the Pulse Generator or manipulate the Lead. Doing so could damage the Lead or your vagus nerve. It could require that the Pulse Generator and Lead be replaced.

10.2. Side Effects Due to Stimulation

Some side effects occur with the VNS Therapy System and stimulation. As a rule, they become less noticeable over time for most patients and, typically, do not result in patients discontinuing VNS Therapy.

Other problems, such as trouble breathing, can occur if device settings are set too high at first or are increased too rapidly, or if the device is started too soon after surgery. If this happens, your doctor can change the device settings.

The VNS Therapy System is not a drug. It does not cause drug-related side effects and does not interact with drugs, including antidepressant medications you may be taking.

10.2.1. Common side effects due to stimulation

These side effects were listed as related to stimulation by the VNS Therapy System. These side effects were reported for 5% or more of the study participants.

During the first year of VNS Therapy, only 3% of the study participants withdrew from the study because of side effects or complications.

	Reported months	
	3	12
Voice alteration	55%	54%
Increased cough	24%	6%
Dyspnea (shortness of breath)	19%	16%
Neck pain	16%	13%
Dysphagia (difficulty swallowing)	13%	4%
Laryngismus (sore, painful throat)	11%	5%
Paresthesia (tingling)	10%	4%
Pharyngitis (inflammation of the throat)	8%	5%
Nausea	7%	2%
Incision pain	5%	6%

After 3 months of VNS Therapy, no new stimulation-related event was reported by more than 1.3% of the study participants.

The most common side effect is hoarseness. Three other common side effects are sore throat, shortness of breath, and coughing. As a rule, these problems typically occur only during stimulation (the ON time of the cycle). A typical stimulation cycle is 30 seconds ON followed by a 5-minute OFF period. Most people who have hoarseness, as well as the other three side effects, tolerate it well and notice it less as time goes on.

 Call your doctor any time hoarseness is painful, constant, or persists.

The following is a partial alphabetical list of the side effects reported during clinical trials of the VNS Therapy System and possibly associated with the VNS Therapy System.

You may experience one or more of them. Talk to your doctor if any one of these items becomes too uncomfortable.

?? Lack of coordination in the voluntary muscles (ataxia)

?? Blood clotting

- ?? Choking sensation
- ?? Device (Pulse Generator and/or Lead) migration or extrusion
- ?? Dizziness
- ?? Duodenal ulcer, gastric ulcer
- ?? Ear pain
- ?? Facial flushing
- ?? Facial paralysis, paresis
- ?? Formation of fibrous tissue, pockets of fluid
- ?? Hiccups
- ?? Irritability
- ?? Left vocal cord injury or paralysis (affects voice)
- ?? Low-grade fever
- ?? Muscle movements or twitching generally associated with stimulation
- ?? Muscle pain
- ?? Ringing in the ears (tinnitus)
- ?? Stomach discomfort
- ?? Tooth pain
- ?? Weight change
- ?? Worsening of asthma and bronchitis
- ?? Throat, larynx spasms (laryngismus)

?? Vomiting

These side effects could *potentially* occur.

?? Aspiration (fluid in the lungs)

?? Damage to nerves or blood vessels in the surgical area, including the carotid artery and jugular vein

?? Foreign body reaction to implants, including possible tumor formation

?? Left hemidiaphragm paralysis

?? Unusual scarring at the incision site

?? Vagus nerve damage

?? Worsening of cardiac abnormalities, including heart rate and rhythm

10.3. Environmental Hazards

Being close to certain types of equipment can affect the Pulse Generator. Move away from or avoid equipment such as transmitting antennas. Ask your doctor before going into places that have warning notices for people not to enter who have heart pacemakers.

10.3.1. Pacemaker Warning signs

Talk to your doctor before going into places with Pacemaker Warning signs.

10.3.2. Small appliances

Properly operating microwave ovens and other small electrical appliances, such as toasters, hair dryers, and electric shavers, should *not* affect the Pulse Generator.

10.3.3. Cellular phones

Cellular phones can affect some implanted cardiac defibrillators and pacemakers. But tests to date show that they do *not* affect the Pulse Generator.

10.3.4. Transmitting devices

Properly operating electrical ignition systems and power transmission lines should *not* affect the Pulse Generator. Sources with high energy levels, such as transmitting antennas, *may interfere* with the device. Move at least 2 meters (6 feet) away from any equipment that interferes with your device.

10.3.5. Antitheft devices, airport security systems, and other metal detectors

Antitheft devices and metal detectors should *not* affect the Pulse Generator or be affected by it. As a precaution, however, move through them at a steady pace; do not linger in the area.

10.3.6. Devices with strong electromagnetic fields

Electrical or electromechanical devices with a strong static or pulsing magnetic field can cause the Pulse Generator to start suddenly. Such devices may include strong magnets, hair clippers, vibrators, and loudspeakers. Keep this type of equipment at least 15 centimeters (6 inches) away from your chest.

If your Pulse Generator stops while you are in a strong electromagnetic field, move away from the source so that the device may return to regular operation.

10.4. Medical Hazards

Medical equipment, procedures, and surgery using certain electrical instruments can affect the VNS Therapy System's operation and sometimes damage the Pulse Generator or Lead.

 Make sure that medical personnel know you have a device implanted in your chest.

 Always call your doctor before you have any medical tests. Precautions may be needed.

10.4.1. Routine diagnostic procedures

Most routine diagnostic procedures, such as diagnostic ultrasound and radiography (x-rays), should *not* affect the VNS Therapy System.

10.4.2. Mammography

Because the Pulse Generator is in your chest, you may need to be specially positioned for a mammogram. Otherwise, the device may be seen as a shadow on the mammogram. It could make a

lesion or lump in that area hard or even impossible to detect. Make sure that your doctor and the mammography technician are aware of the implanted device.

10.4.3. Radiation treatment

Treatment with radiation, cobalt machines, and linear accelerators *may* damage the Pulse Generator. Note that no testing has been done to date. The effect of radiation on the device is not known. Talk with your doctor if you plan to have radiation treatment.

10.4.4. Magnetic resonance imaging

If you plan to have **magnetic resonance imaging** (MRI), make sure your doctor has this information.

 **Magnetic resonance imaging (MRI) should not be performed with a magnetic resonance body coil in the Transmit Mode.** The heat induced in the Lead by an MRI body scan can cause injury.

If an MRI should be done, use only a transmit-and-receive type of head coil. Magnetic and radio frequency (RF) fields produced by MRI may change the Pulse Generator settings (change to reset parameters) or activate the device.

Stimulation has been shown to cause the adverse events reported in the “Adverse Events” section of this manual. MRI compatibility was demonstrated using a 1.5T General Electric Signa Imager and Model 100 Pulse Generator only. Testing on this imager as performed on a phantom indicated that the following Pulse Generator and MRI settings can be used safely without adverse events.

?? Pulse Generator output: programmed to 0 mA for the MRI procedure, and afterward, retested by performing the Lead Test diagnostics and reprogrammed to the original settings

?? Head coil type: transmit and receive only

?? Static magnetic field strength: ? 2.0 tesla

?? Specific-rate absorption (SAR): ? 1.3 W/kg for a 70-kg (154.5-lb) patient

?? Time-varying intensity: ? 10 tesla/sec

Use caution when other MRI systems are used, since adverse events may occur because of different magnetic field distributions.

 No scan in which the radio frequency (RF) is transmitted by the body coil should be done on a patient who has the VNS Therapy System. Thus, protocols must not be used which utilize local coils

that are RF-receive only, with RF-transmit performed by the body coil. Note that some RF head coils are receive only, and that most other local coils, such as knee and spinal coils, are also RF-receive only. **These coils must not be used in patients with the VNS Therapy System.**

10.4.5. Other procedures

External cardiac defibrillation and other procedures for heart problems, as well as extracorporeal shockwave lithotripsy, diathermy, and electrocautery, *may damage* the Pulse Generator. If you had any of these procedures and your doctor did not know about it, have the Pulse Generator checked.

While *diagnostic* ultrasound should *not* affect the VNS Therapy System, *therapeutic* ultrasound therapy *could* damage the Pulse Generator or inadvertently harm you by concentrating the therapy.

10.5. Interference with Other Devices

While the Pulse Generator is stimulating or being set or tested, it may briefly interfere with nearby equipment. If this happens, move at least 2 meters (6 feet) away from such equipment.

10.5.1. Radios and hearing aids

The Pulse Generator can interfere with devices operating in the 40 kHz to 100 kHz range. Hearing aids and transistor radios operate in this range. In theory, the Pulse Generator could affect

them, but no effects have yet been reported. No detailed testing has been done, so the effects are unknown.

10.5.2. Implanted devices

The Pulse Generator may affect other implanted medical devices, such as cardiac pacemakers and implantable defibrillators. Possible effects include sensing problems. These could lead to inappropriate responses from the Pulse Generator.

10.5.3. Credit cards and computer disks

The VNS Therapy Magnets are very strong. They *can* damage televisions, computer disks, credit cards, and other items that are affected by strong magnetic fields. Keep your Magnet at least 25 centimeters (10 inches) away from any of these items. **Do not carry or store the Magnets near them.**

11.DEVICE DESCRIPTION

The Pulse Generator and Lead are made from materials long used in heart pacemakers and other implanted medical devices. The VNS Therapy System contains no latex. The Pulse Generator is about the size and shape of a large pocket watch. The Lead is about the size and shape of a 43-centimeter-long (16-inch) piece of wire.

11.1. Battery Life

The Pulse Generator battery can last from 1 to 16 years. The lifespan depends on these factors.

?? Pulse Generator model

?? Settings your doctor chooses

?? Interaction of the Lead and vagus nerve over time

At typical settings, battery life ranges from 6.6 to 10 years. Ask your doctor for more details about your device and settings. When a battery runs out, VNS Therapy stops. At that point, the Pulse Generator must be replaced. The Pulse Generator can be replaced in an outpatient

operation. The operation uses local anesthesia, and most of the time, takes about 1 hour.

 If stimulation **feels different or suddenly stops**, call your doctor. Have the Pulse Generator tested. Your depressive symptoms may increase when VNS Therapy stops.

 All Magnets can **lose their effectiveness** over time. If you suspect that either of your Magnets is not working, call your doctor.

11.2. Device Disposal

Explanted Pulse Generators should be sent to Cyberonics for safe disposal.

Returned VNS Therapy System parts become the property of Cyberonics.

 People with a VNS Therapy Pulse Generator implanted should not be cremated until the device has been removed. The temperatures required for cremation could cause the device to explode.

12. CYBERONICS' PATIENT WARRANTY AND SAFETY LISTING

Government agencies require makers of implantable devices to contact people in case of emergencies related to the device. Cyberonics has a listing of people who have had the Pulse Generator and Lead implanted. The information is kept in confidential files. It is a permanent record of the implantation surgery. Cyberonics will release a file only if required by law.

 Please send Cyberonics **a change of address notice** if you move.

13. FREQUENTLY ASKED QUESTIONS

Patients and their family members often ask these questions.

How do most people respond to VNS Therapy? When the device was tested in the clinical trials, the depressive symptoms decreased for most patients. Some patients had no change in depressive symptoms. Some patients do not have a decrease in depressive symptoms until after they have had several months of VNS Therapy.

Can I know if I will be helped before I am implanted with the Pulse Generator and Lead? At this time, there is no way to predict what your response will be.

What are the results of the VNS Therapy clinical trials? Your doctor can give you information about the clinical trials (research studies).

What is the implantation surgery like? You will be given a general or local anesthetic. The operation usually takes 1 to 2 hours. The operation will be done with you as an outpatient (you go home the same day) or you may stay in

the hospital overnight. Ask your surgeon to tell you more about the anesthetic, the operation, and the hospital stay so that you will know what to expect.

Are there risks linked with the surgery? Any surgery has some type of risk. It is important that you discuss this question with your surgeon.

Will the scars be noticeable? Each person has different healing and scarring results. You should expect some scarring from surgery. Most people do not think the scarring after surgery is a major concern. If this is a special concern for you, discuss it with your surgeon.

Will people be able to see the implanted device through my skin? The Pulse Generator is shaped like a disk. The Model 101 is 5.4 centimeters (2.1 inches) across and 1 centimeter (0.4 inch) thick; it weighs about 38 grams (1.34 ounces). The Model 102 is 5.2 centimeters (2.0 inches) across and 0.7 centimeter (0.27 inch) thick; it weighs about 25 grams (0.88 ounce). The Model 102R is 5.2 centimeters (2.0 inches) by 5.8 centimeters (2.3 inches) and 0.7 centimeter (0.27 inch) thick, weighing about 27 grams (0.95 ounce). If you have a small frame or

are very thin, the device may be visible below your left collarbone.

What happens after the surgery? Your doctor will set the treatment settings of your device. If the stimulation feels uncomfortable, your doctor can change it to make you more comfortable. The doctor will use the Programming Wand to check and fine-tune your stimulation settings at each visit.

Will I be able to tell when the stimulator is on? Many people note a tingling feeling or a change in their voice (hoarseness) during stimulation. In general, most side effects become less noticeable over time.

What are the side effects of VNS Therapy? The most common side effects reported for the VNS Therapy System are a tingling sensation in the neck and mild hoarseness in the voice, both of which occur only during stimulation, a cough, and dyspnea (shortness of breath). Other less common side effects are discussed in the “Complications” and “Side Effects” sections of this manual. In general, most side effects become less noticeable over time.

When should I use the Magnet? Use the Magnet to stop stimulation.

How does the Magnet work? The Pulse Generator has a sensor (the Reed Switch) that recognizes the Magnet and stops stimulation.

Can any magnet be used? Only the Cyberonics Magnet should be used with your VNS Therapy System. If you lose your Magnet or require extra Magnets, contact your doctor. In an emergency, you may try other strong magnets. The use of other, non-Cyberonics magnets will not harm the VNS Therapy System. But there is no way to know whether a magnet other than the Cyberonics Magnet will work.

What if the Magnet is accidentally kept in place over the Pulse Generator for an extended period? No stimulation will be delivered while the Magnet is kept over the device. Stimulation will resume only after the Magnet is removed.

Is it possible to stop all stimulation using the Magnet? Yes. To stop stimulation, hold the Magnet over the Pulse Generator and keep it there. Use this method if you have unusual or

painful stimulation. Then call your doctor right away. The Magnet will stop all stimulation while it is held in place. You may need to secure the Magnet by taping it over the implanted device.

Who should carry the Magnet? You should carry the Magnet so that it is always with you. You may also want your family members or caregivers to have access to a Cyberonics Magnet.

Is the Magnet an environmental hazard? The Cyberonics Magnet can damage computer disks, credit cards, watches, and other items affected by strong magnetic fields. Keep your Magnet at least 25 centimeters (10 inches) away from any of these items. Do not store Magnets near such items.

Other Questions? If you have other questions about the VNS Therapy System, any of its parts, or VNS Therapy in general, talk to your doctor.